

Immunoinformatics

–

Computational Immunology

VISIT...

LANZAROTE
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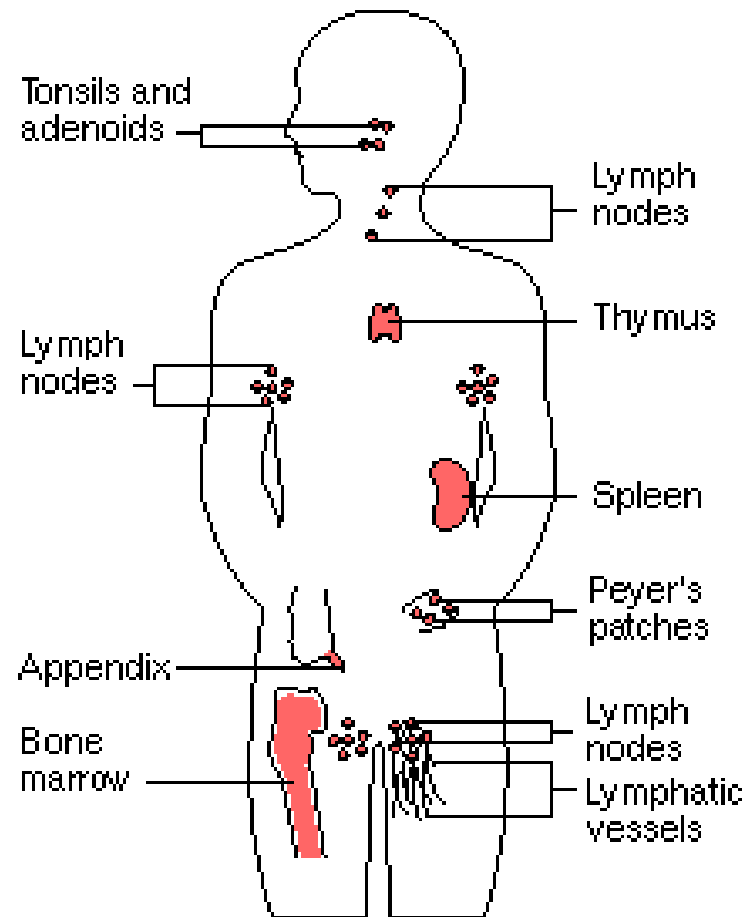
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Immune System Presentation

Immune System

- Composed of many interdependent
 - cell types
 - organs
- Collectively protect the body

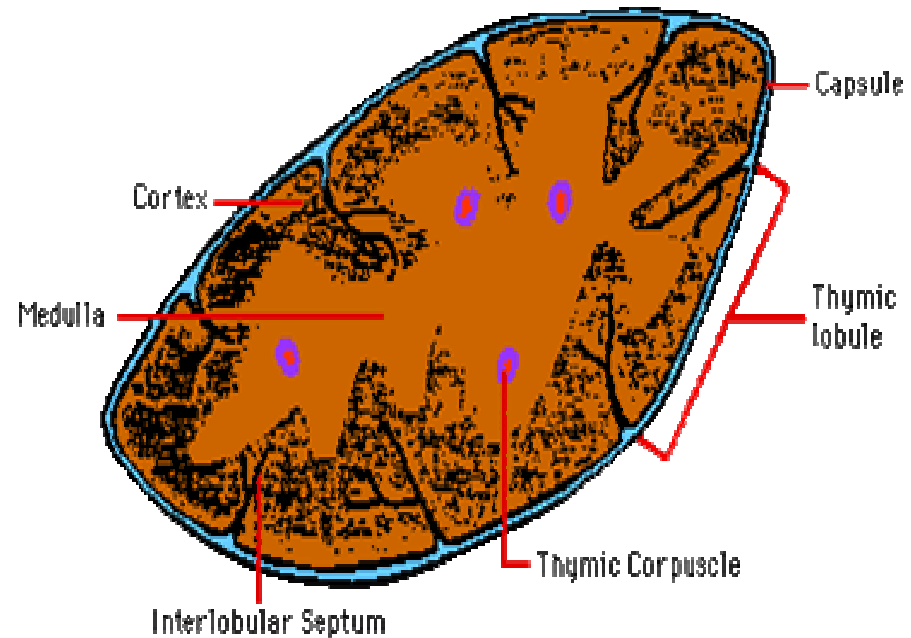


Self/Non-Self

- Every cell display a marker based on the major histocompatibility complex (MHC)
- MHC may be of three different classes
 - MHC I, MHC II, MHC III
- Any cell not displaying this marker is treated as non-self and attacked.

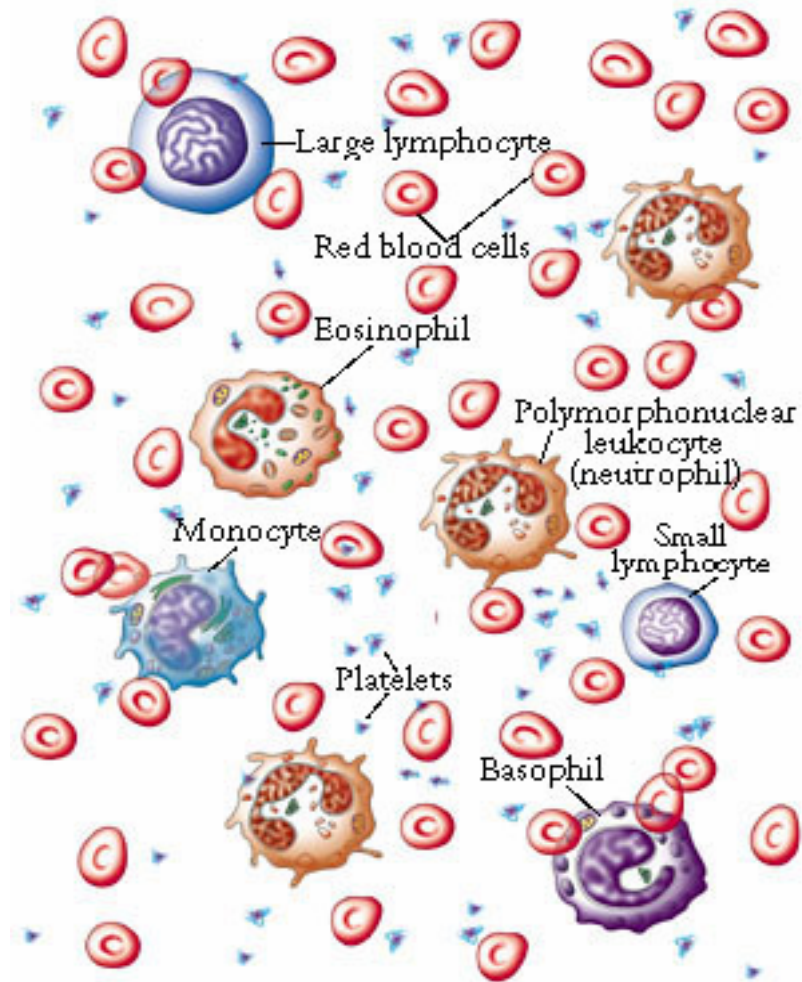
Main Organs

- Bone Marrow
 - Immune system's cells production
- Thymus
 - Maturation of T cells
- Spleen
 - Immunologic blood filter and RBC recycle unit
- Lymph Nodes
 - Immunologic filter for the lymph

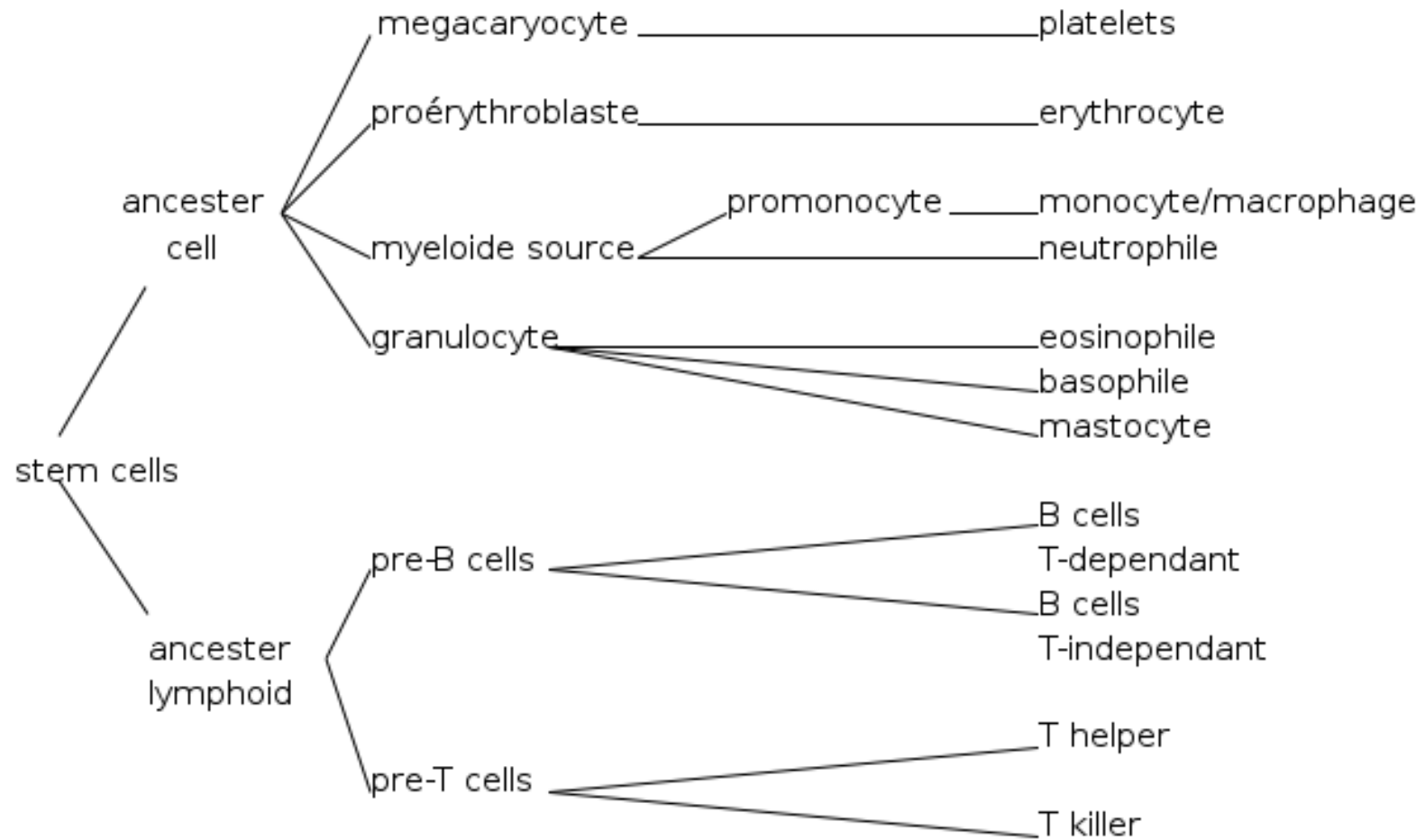


Main Cells

- Blood cells are manufactured by stem cells in the bone marrow
- The process is called hematopoiesis
- Three different types of blood cells
 - Erythrocytes (RBC)
 - Leukocytes (WBC)
 - Granulocytes
 - Agranulocytes
 - Thrombocytes (platelets)



Main Cells (2)



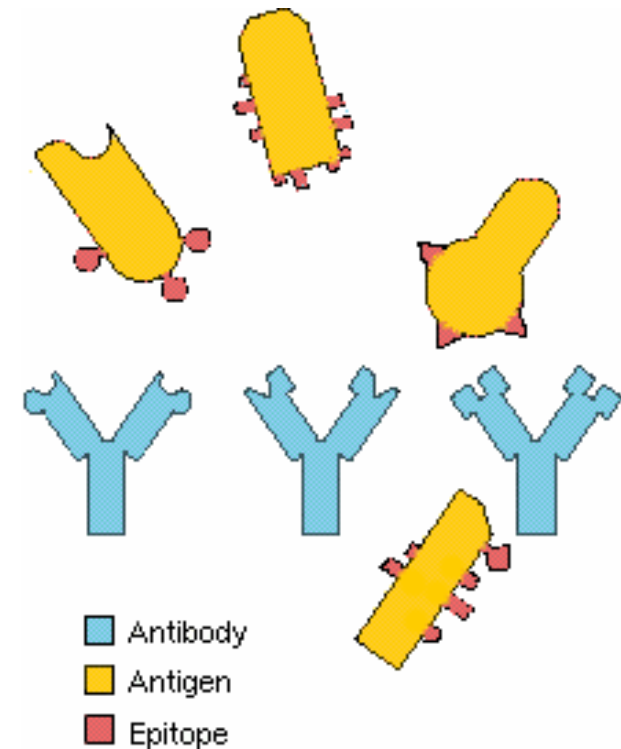
Main Cells (3)

- Lymphocytes
 - T
 - TH (CD4+ T)
 - TK (CD8+ T)
 - B
 - NK
- Granulocytes
- Macrophages
- Dendritic Cells



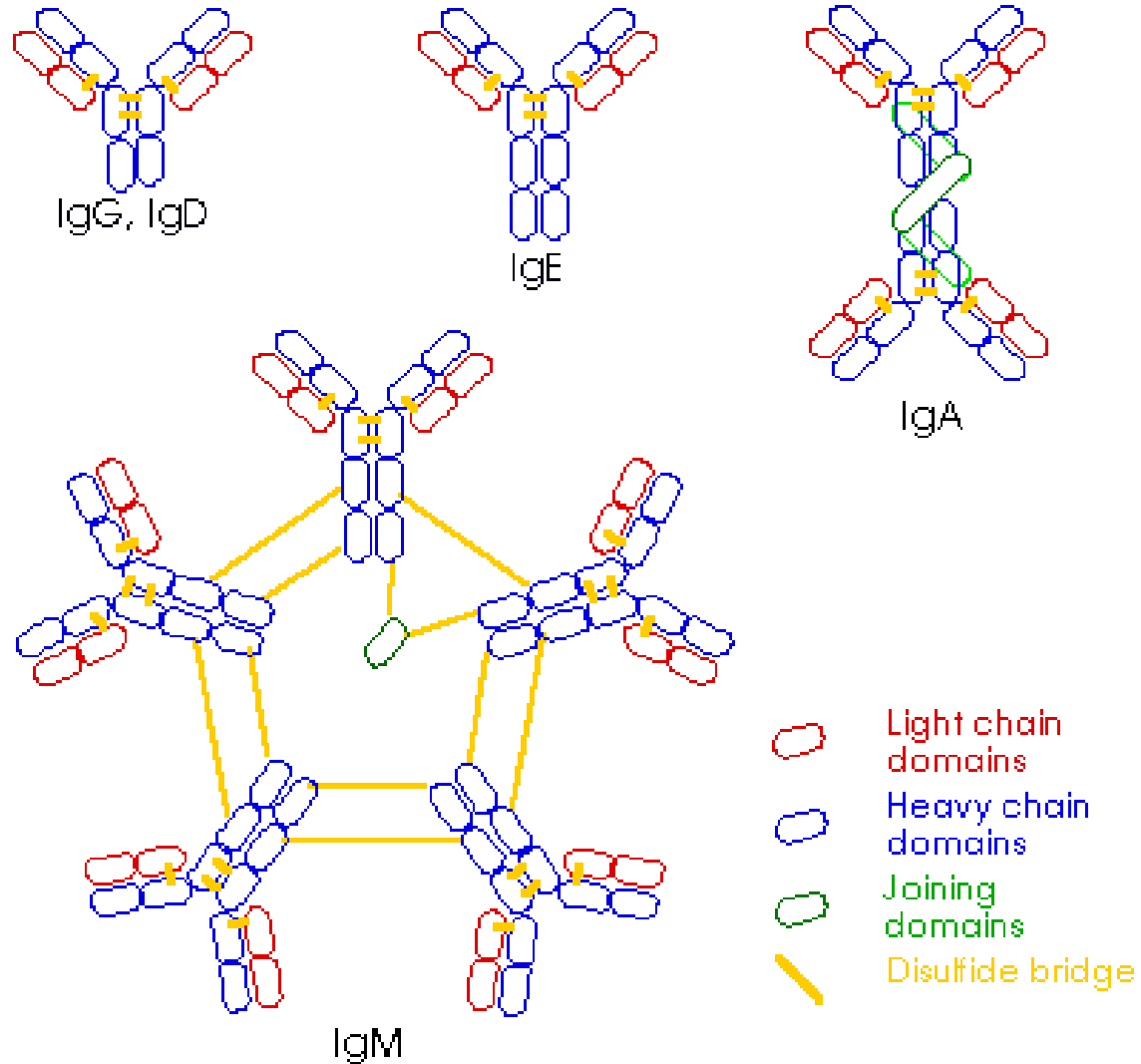
Antibody

- Antigen: substance that elicits an immune response
- Antibody: complex protein secreted by B cells
 - Tagging: Coat the foreign invaders to make them attractive to the circulating scavenger cells
 - Complement fixation: Combine with antigens and a circulating protein in the blood that cause lysis
 - Neutralization: Coat viruses and prevent them from entering cells
 - Agglutination: massively clump to the antigen
 - Precipitation: force insolubility and settling out of solution

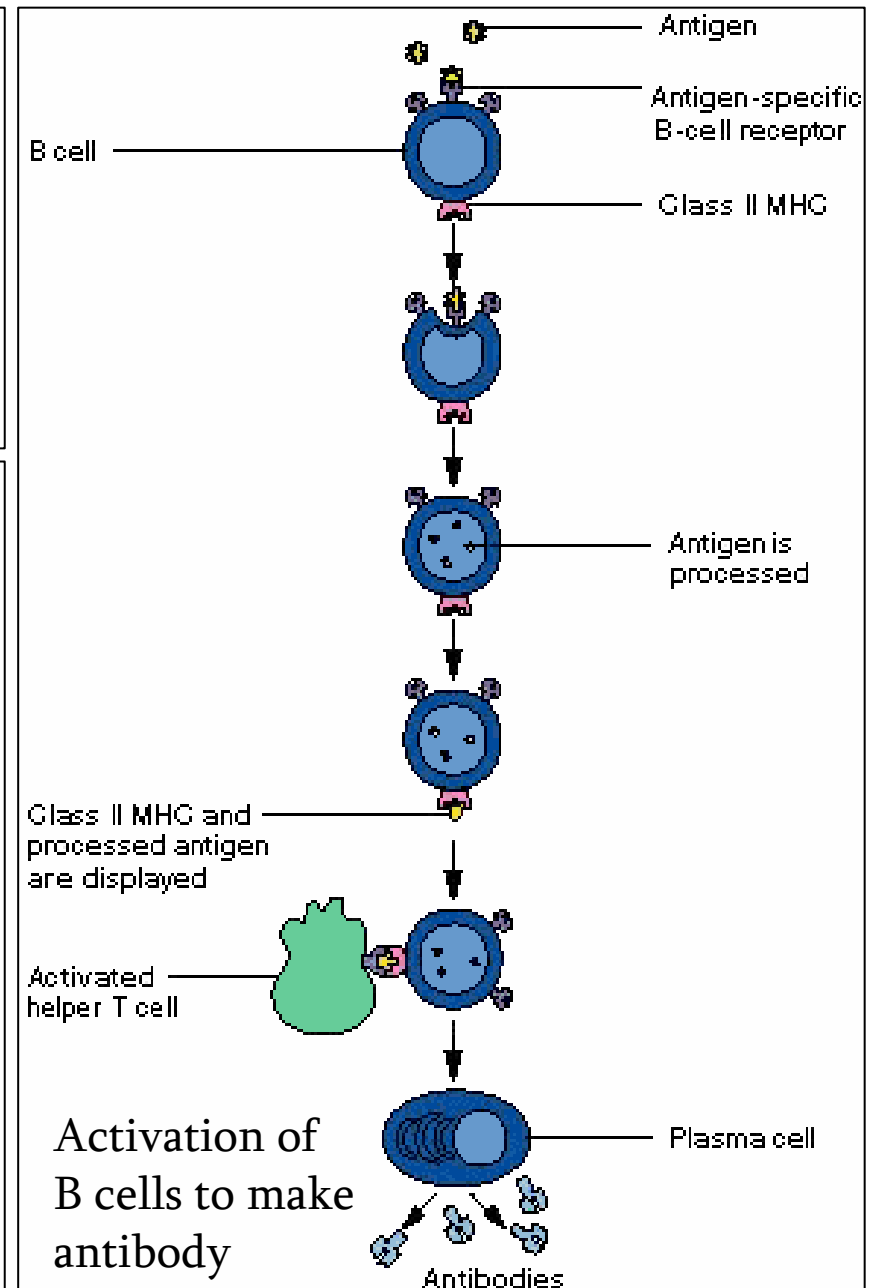
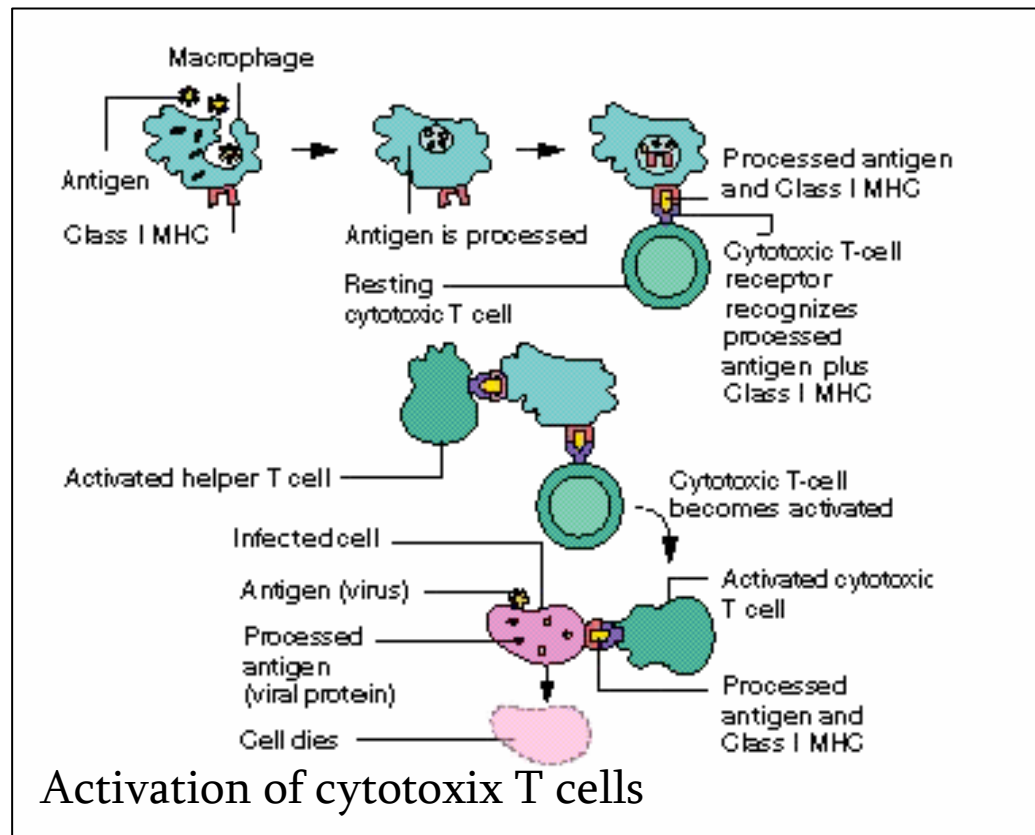
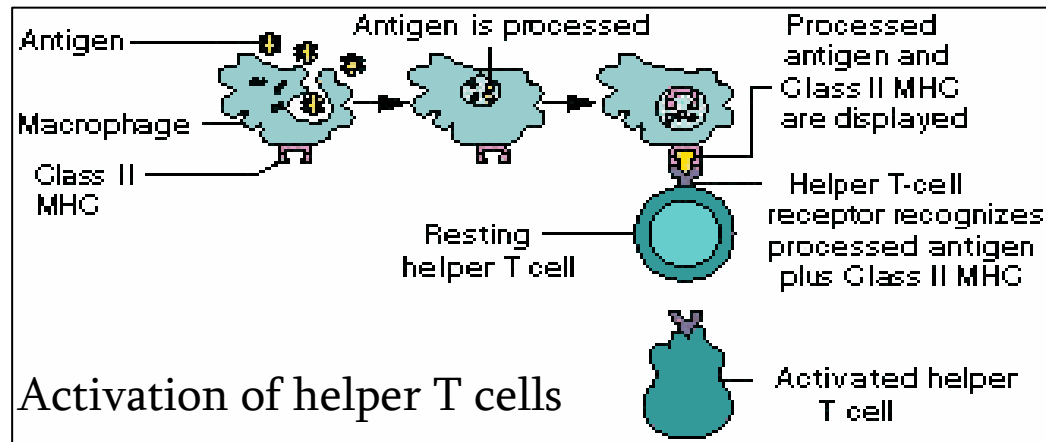


Antibody (2)

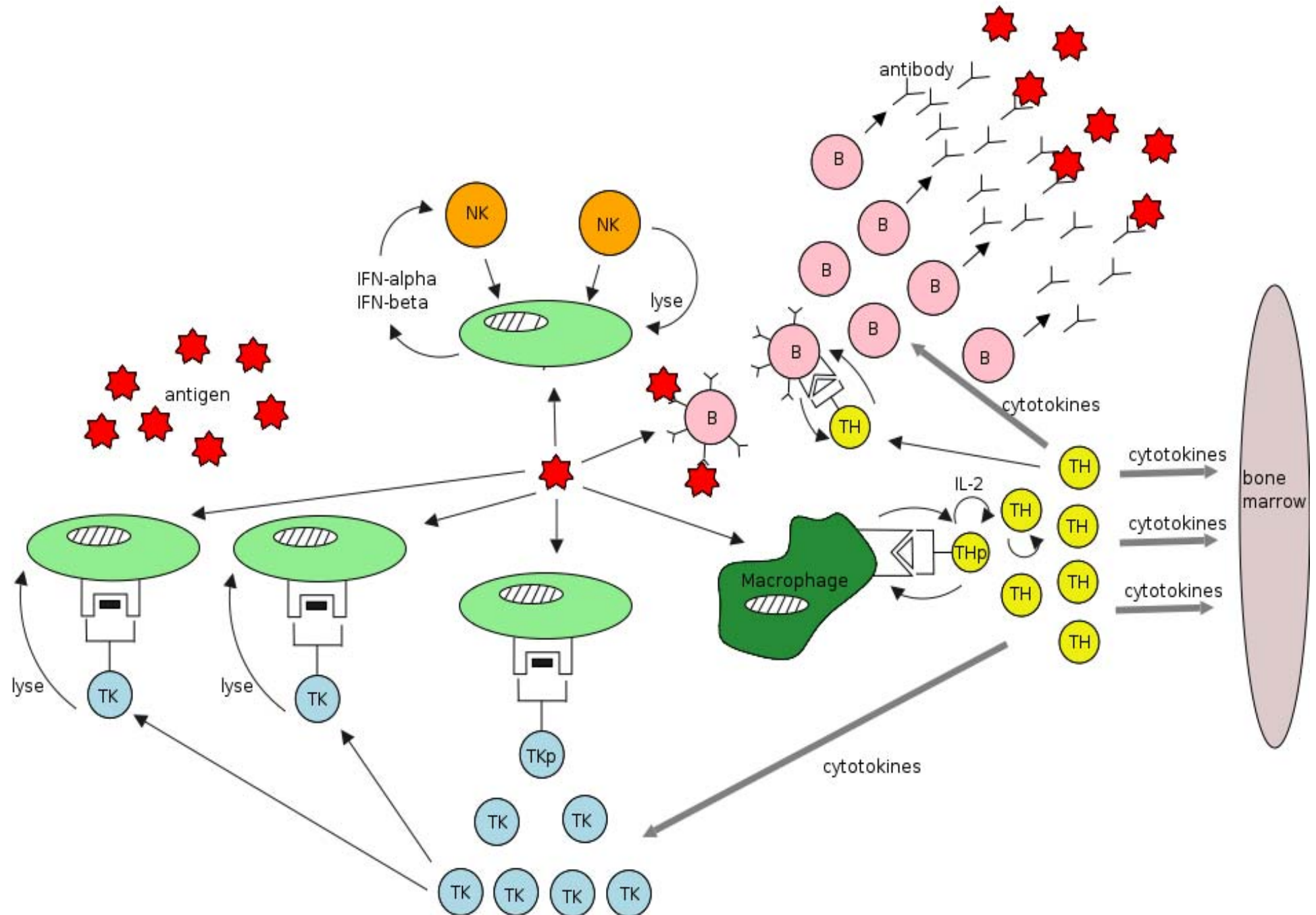
- IgG-75%
- IgA-15%
- IgM-7.5%
- IgD-1%
- IgE-0.002%



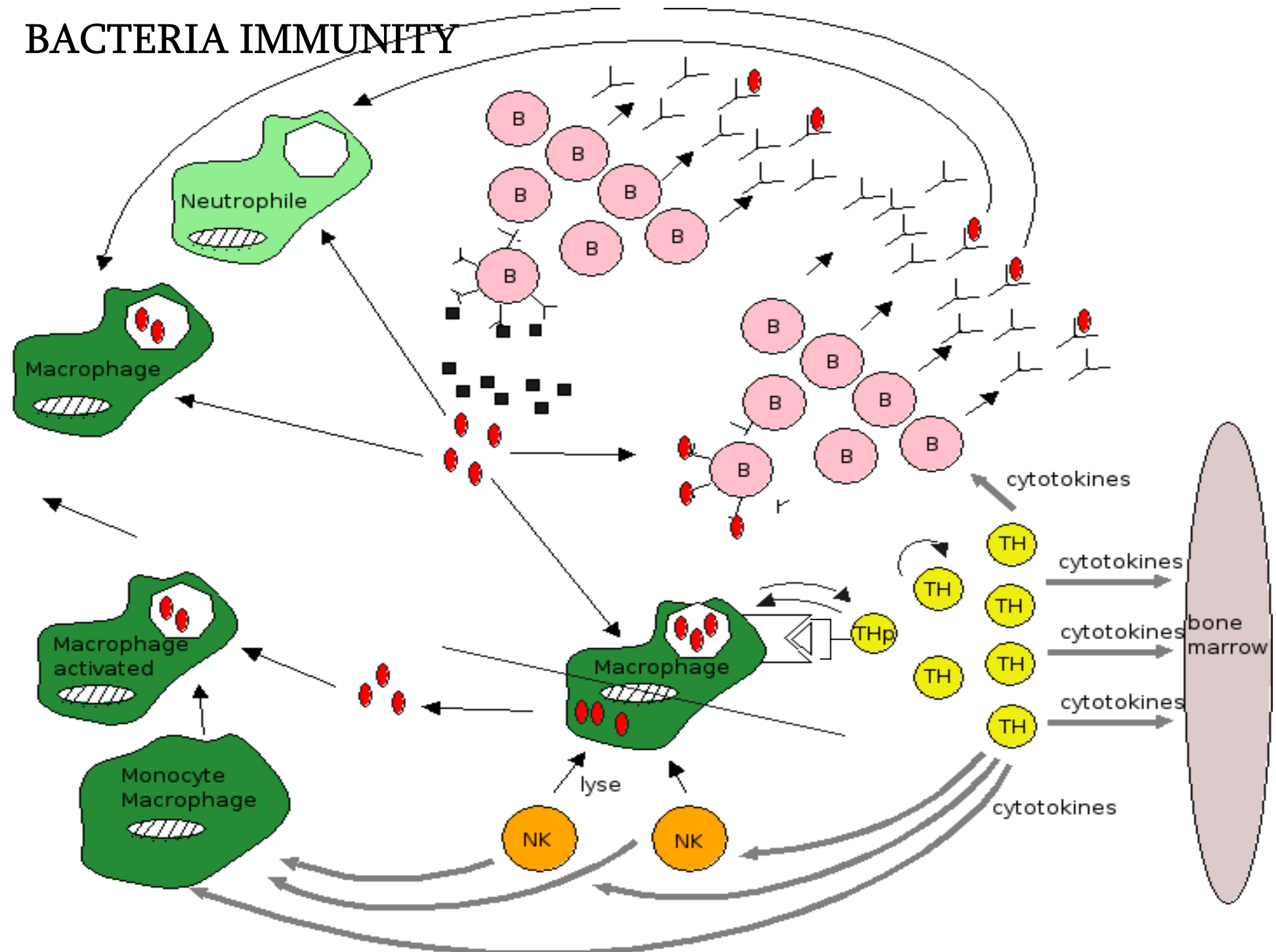
Activation of WBC



VIRUS IMMUNITY



BACTERIA IMMUNITY



Cell-mediated/Hummmoral Immunity

- Cell-mediated immunity
 - T cells (lymphocytes) bind to the surface of other cells that display the antigen and trigger a response. The response may involve
 - other lymphocytes and
 - any of the other WBC
- Hummmoral immunity
 - Antibodies, dissolved in blood, lymph, and other body fluids bind the antigen and trigger a response to it.

Innate/Acquired-Adaptive Immunity

- Innate immunity rely on a global distinction of self/non-self recognition
 - Instantaneous
 - Non specific
 - Non adaptative
 - Memory less
- Adaptative immunity involve the cell-mediated and hummoral response.
 - Time limited to the eradication of the antigen
 - Specific to the given antigen
 - Adaptativ
 - Memory full

Immunologic Memory

- First Response (4-5 days)
 - First adaptive response against a given antigen
- Secondary Response (1 day)
 - Shorter lag time
 - More rapid buildup
 - Higher overall level of response
 - Better fit to the invading antigen
 - Utilizes IgG instead of IgM

Immunoinformatics

Chair's introduction

Hans-George Rammensee

Immunoinformatics the new kid in town

Vladimir Brusic and Nikolai Petrovsky

3 Fields

- Theoretical immunology or immunoinformatics
 - Hard
 - Hard facts, can be verified by experience
 - Semi-soft
 - Algorithms and parameters used to ‘create’ the hard part
 - Soft
 - Can never be tested with hard facts

Combinatorial Science

- Immunoinformatics also known as computational immunology
- Astounding diversity of immune system components
- Complexity of the regulatory pathways
- Complexity of the network-type interactions

Immunology Databases

- Management and analysis of immunological data plays a major role in immunoinformatics
- The appropriate use of informatics technique greatly improve the efficiency of immunology research

Standards

- Data Standards
 - [IUPAC/IUBMB](#)
 - [Gene ontology consortium](#)
 - [Immunogenetics ontologies and nomenclature for immunoglobulins](#)
- Data quality
- Accuracy of computational methods

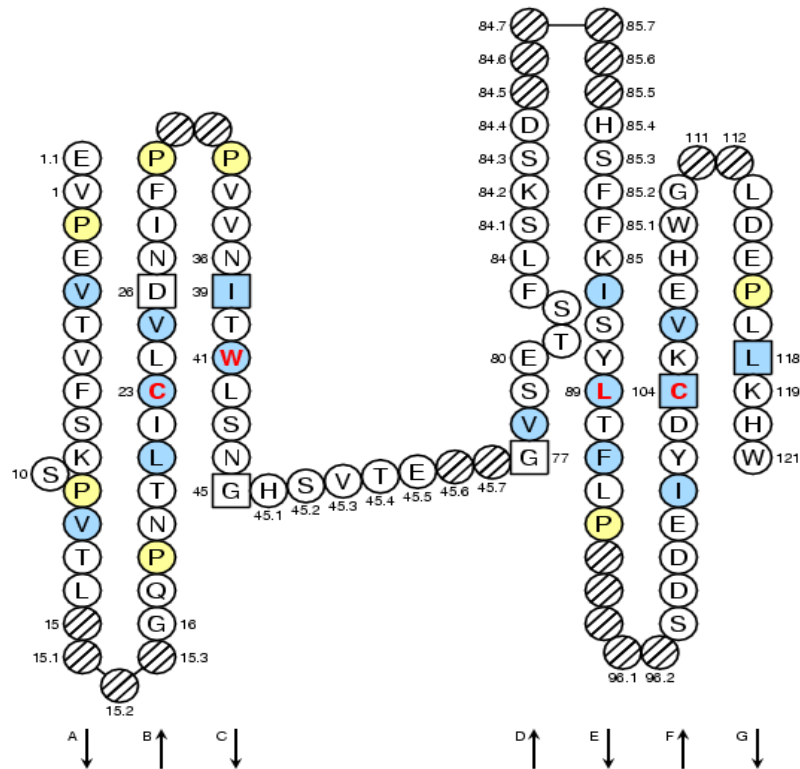
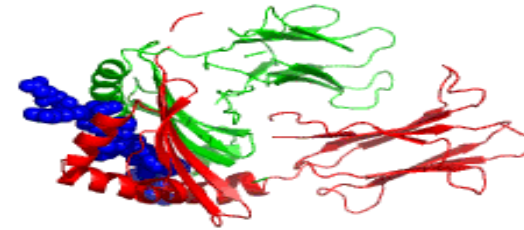
IMGT, the international ImMunoGeneTics information system



Marie-Paule Lefranc
Université de Montpellier II

IMGT Databases

- IMGT/LIGM_DB
- IMGT/3Dstructure-DB
- IMGT/MHC_DB
- IMGT/PRIMER-DB
- IMGT/GENE-DB



IMG_T Databases (2)

- IMG_T/LIGM-DB
 - 75000 nucleotide sequences from 105 species
- 6 people working full time on annotation
- Daily updates and curation
- Multilevel annotation
- Standardized keywords

IMGT Databases (3)

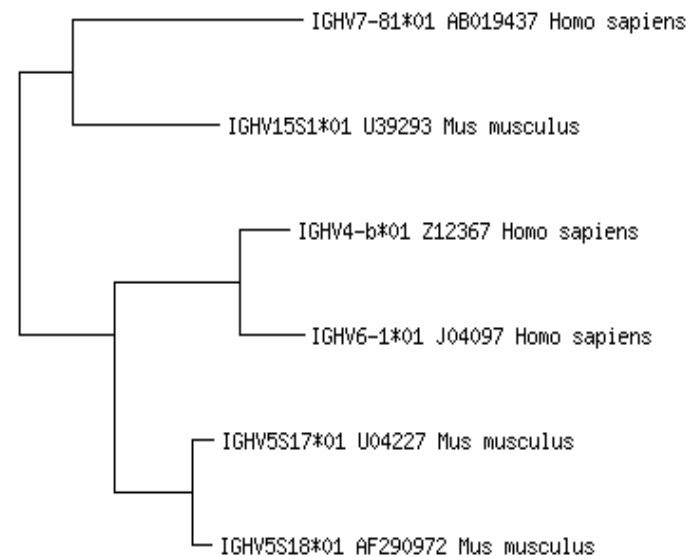
- Distributed by anonymous FTP
 - CINES, EBI, IGH, Institut Pasteur, ...
 - Flat files
- BLAST and FASTA searchable
- Relational Database Structure
 - Sybase for LIGM, GENE and PROTEIN
 - MySQL for 3DStructure and PRIMER
- IMGT API

IMGT Web Ressources

- IMGT Scientific chart
 - Standardized keywords
 - Standardized sequence annotation
 - Standardized IG and TR gene nomenclature
- IMGT Repertoire
- IMGT/V-QUEST
- IMGT/JunctionAnalysis
- IMGT-ONTOLOGY

IMG/PhyloGene tree with branch lengths

The phylogenetic tree found by NJ from your selected sequences and rooted using the midpoint procedure is the following :



🔗 Display the same tree

🔗 Root this tree using an outgroup

🔗 Root this tree using the midpoint method

🔗 Return to the sequence selection (to add an outgroup for example)

🔗 Download the tree in Newick format

Discussion

- Data mining through multiple databases
- Database Access
- SRS
- Webservices
- Workflows

[Reset](#)

[Quick Search](#)

Search Options

1. **Select** the **databanks** you want to search
2. Enter your **search terms** in the **Quick Search** box, or choose a **query form** from below

[Standard Query Form](#)
[Extended Query Form](#)

You can **browse** through all the **entries** in any **databanks**. First, **select** the **databanks** you want to browse, then click:

[Browse Entries](#)

Tips

► bookmark this [link](#) to return to your project

Available Databanks

☒ [Expand all](#) ☐ [Collapse all](#)

Show databanks tooltips: ☒

+ EMBOSS Results

- Sequence databanks - complete

- ☒ [all](#) ☐ [EMBL](#) ☐ [RefSeq](#) ☐ [RefSeq Protein](#) ☐ [TREMBL](#) ☐ [SWALL](#)
☐ [SWISSPROT](#) ☐ [PIR](#) ☐ [REMTREMBL](#) ☐ [UniProt](#) ☐ [IPI](#)
☐ [ENSEMBL](#)

+ Sequence databanks - subsections

- SeqRelated

- ☒ [all](#) ☐ [PROSITE](#) ☐ [PROSITEDOC](#) ☐ [PRINTS](#) ☐ [PFAMA](#)
☐ [PFAMB](#) ☐ [SWISSPFAM](#) ☐ [PFAMHMM](#) ☐ [PFAMSEED](#)
☐ [EPD](#) ☐ [DBEST](#) ☐ [UNIGENE](#) ☐ [UNIGENESEQ](#)
☐ [UNIGENEUNIQ](#) ☐ [INTERPRO](#) ☐ [IPRMATCHES](#) ☐ [MARKERS](#)
☐ [MARKERSHQ](#) ☐ [MARKERSLQ](#)

+ Tool Results

- Protein3DStruct

- ☒ [all](#) ☐ [PDB](#) ☐ [PDBFINDER](#)

- Genome

- ☒ [all](#) ☐ [LOCUSLINK](#)

- Mutations

- ☒ [all](#) ☐ [OMIM](#)

- Metabolic Pathways

- ☒ [all](#) ☐ [ENZYME](#) ☐ [PATHWAY](#) ☐ [LENZYME](#) ☐ [LCOMPOUND](#) ☐ [LREACTION](#)

- Others

- ☒ [all](#) ☐ [TAXONOMY](#) ☐ [GENETICCODE](#) ☐ [REBASE](#) ☐ [AAINDEX](#)
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WSDL

Updated: 25/08/04

Web Services Description Language (WSDL), a standard method of describing Web Services and their capabilities. The following is a list of WSDL URLs:

Web Services

Service	URL
WSDBfetch	http://www.ebi.ac.uk/ws/services/urn:Dbfetch?wsdl
WSFasta	http://www.ebi.ac.uk/ws/WSFasta.wsdl
WSWUBlast	http://www.ebi.ac.uk/ws/WSWUBlast.wsdl
WSInterProScan	http://www.ebi.ac.uk/ws/WSInterProScan.wsdl

The future of computational modelling and prediction systems in clinical immunology

*Nikolai Petrovsky, Diego Silva and
Vladimir Brusic*

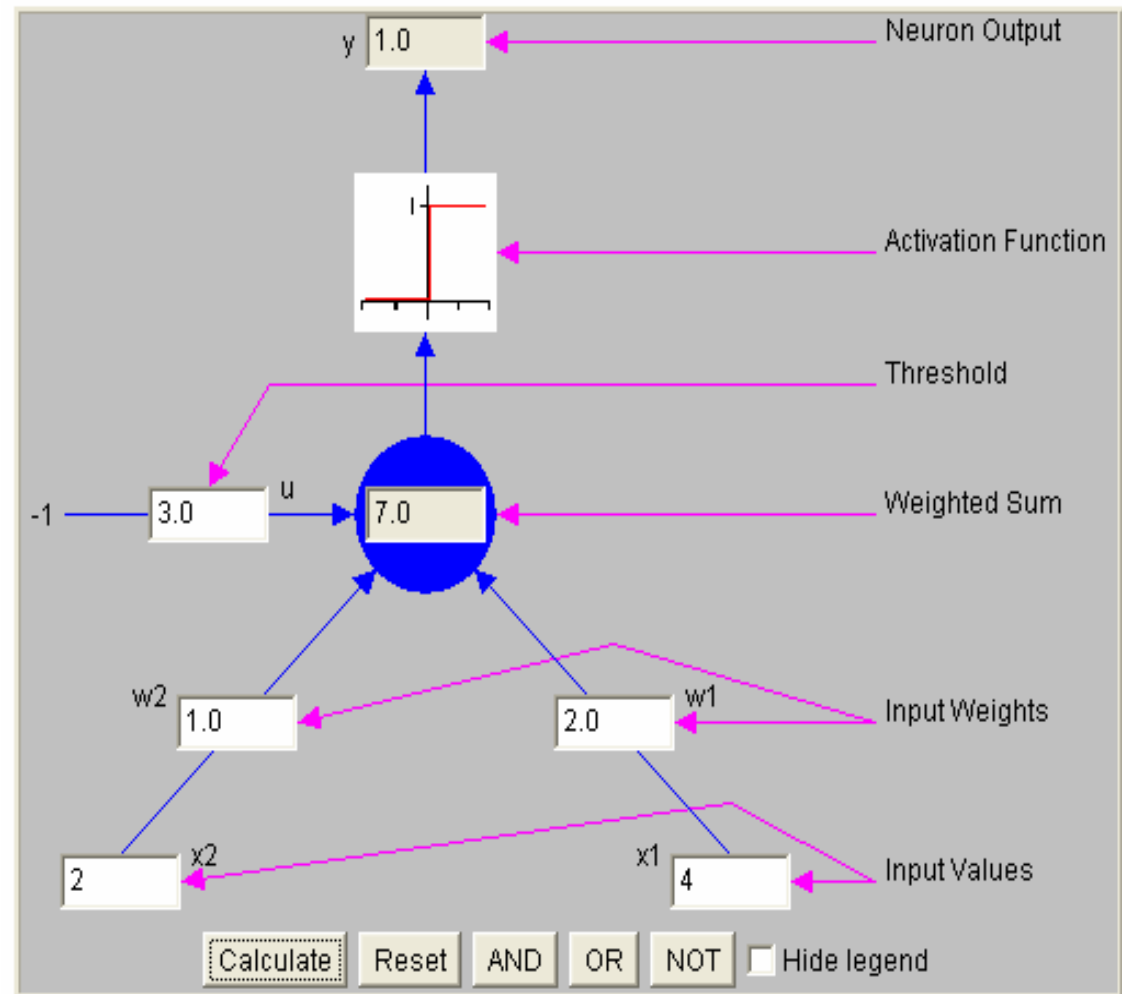
Immunoinformatics In Improving Transplantation Outcomes

- ANN 6 month graft survival prediction
 - MLFF (3 layer feed forward) Neural Network
 - 84.95% accuracy for succeseful transplants
 - 71.70% accuracy for unsuccessful transplants
- Useful clinical tool improving transplantation outcome
- Acceptance by clinicians

ANN Neuron Model

- Input: external stimuli
- Weight: determine the contribution of each entry
- Threshold: bias value, may be seen as a supplementary input value with value -1.

$$y = f\left(\sum_{i=1}^n w_i x_i - u\right) = f\left(\sum_{i=0}^n w_i x_i\right)$$

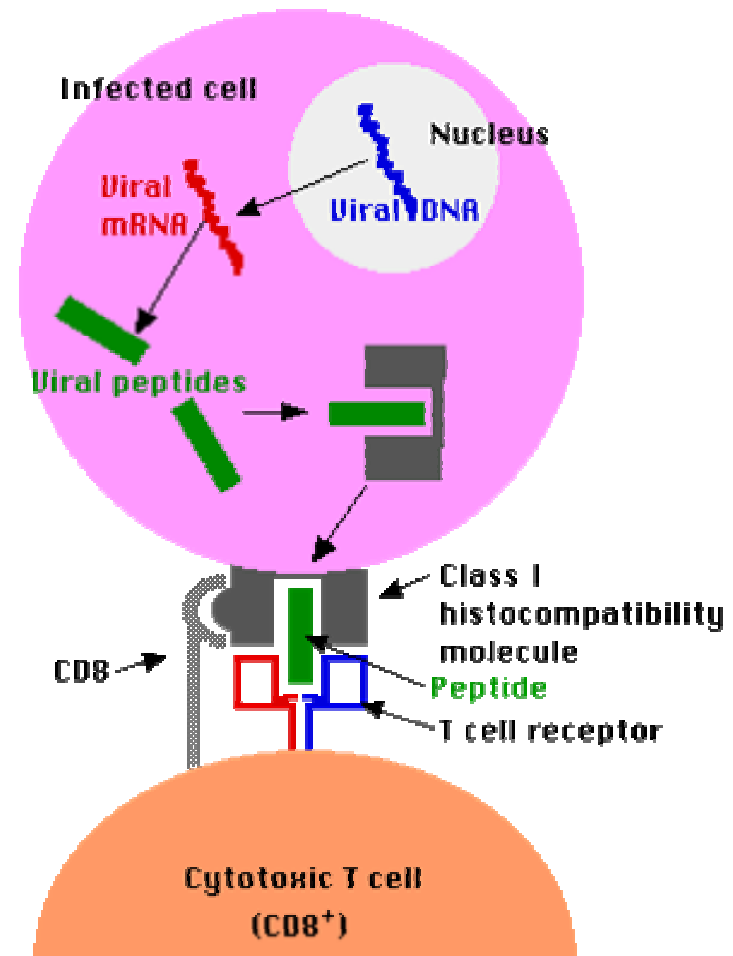


Human Immune Disease-Gene Identification

- Orthologues genes identification
 - Mouse vs Human
- RIKEN database
- FANTOM 3
- Orthogonal gene search

Antigen Presentation Pathways

- TAP(Transporter Associated with antigen Processing)
- HLA-binding peptides with affinity to TAP
 - 15% for HLA-B*5401
 - 100% for HLA-B*2703



Prediction Of Allergeneicity

- Allergenic potential aspect:
 - allergenic Immunogenicity
 - Likelihood of an IgE or T cell response to a particular allergen
 - Cross-reactivity
 - Ability of an IgE clonotype or a T cell clone, which was previously induced by one allergen, to react with another allergen
- [Allergens database](#)
- Structural bioinformatics
- Homologue sequence search

Discussion

- Immunoinformatics accelerate the knowledge acquisition in clinical immunology
- Bioinformatics has broad applicability to immunology
- Development of *in-silico* models of entire systems – towards a virtual immune system

Summary

- Immunoinformatic is very complex and can be seen as a combinatorial science
- Available data come at an exponential rate
- Immunoinformatic rely on data and discoveries from other bioinformatics domains and informatic
- Workflow may become very important in the futur
- Semantic is very important XML may be very useful
- Clinical use of immunoinformatic solutions may be difficult to get accepted

References

- Books

- Immunoinformatics: bioinformatics strategies for better understanding of immune function, Novartis Foundation, ISBN 0-470-85356-5
- Article paru dans la *Revue Française des Laboratoires* 2000, 319 : 14.
- *Le Livre Blanc de l'Immunologie Médicale* Société Française d'Immunologie, 1996
- Cours d'immunologie du Dr. Chevailler, Faculté de Médecine d'Anger
- Introduction à l'immunologie, Fischberg-Azimi, Université de Genève